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**Acceptability and Preferences for Hypothetical Rectal Microbicides among a Community
Sample of Young Men who have Sex with Men and Transgender Women in Thailand: A
Discrete Choice Experiment**

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Running head: Rectal microbicide acceptability among YMSM and transgender women in
Thailand

ABSTRACT

Rectal microbicides (RM) may offer substantial benefits in expanding HIV prevention options for key populations. From April to August 2013, we conducted Tablet-assisted Survey Interviewing, including a discrete choice experiment, with participants recruited from gay entertainment venues and community-based organizations in Chiangmai and Pattaya, Thailand. Among 408 participants, 74.5% were young men who have sex with men (YMSM), 25.5% transgender women, with mean age = 24.3 years. One-third (35.5%) had \leq 9th grade education; 63.4% engaged in sex work. Overall, 83.4% reported they would definitely use a RM, with more than twofold higher odds of choice of a RM with 99% versus 50% efficacy, and significantly higher odds of choosing gel versus suppository, intermittent versus daily dosing, and prescription versus over-the-counter. Sex workers were significantly more likely to use a RM immediately upon availability, with greater tolerance for moderate efficacy and daily dosing. Engaging key populations in assessing RM preferences may support biomedical research and evidence-informed interventions to optimize RM effectiveness.

Keywords: Rectal microbicide; Young men who have sex with men (YMSM); Transgender women; Male sex workers; HIV; Discrete choice experiment; Thailand

INTRODUCTION

Sustained high HIV prevalence (from 25-31%) and incidence (5.3 – 5.5 per 100 person-years) among men who have sex with men (MSM) documented in Bangkok from 2006 to 2013 indicate an urgent need for new prevention options (1). This need is particularly pressing for young MSM (YMSM), who are at the highest risk for infection (1). High HIV incidence (8.2 per 100 person-years) is also evident among gay and other MSM, and transgender persons, in Chiang Mai (2). HIV prevalence among transgender women in Thailand is estimated at 12.5% to 13.5% (3,4). Globally, both men (5) and transgender women (6,7) who engage in sex work are at heightened risk for HIV infection. Limited data from Thailand identified HIV prevalence of 18.8% in a study of male sex workers in Bangkok (8) and 17% among transgender women sex workers in three Thai cities (9).

Compounding the challenges for HIV prevention among YMSM and transgender women in Thailand are evidence of high prevalence (9.2%) of transmitted drug resistance among HIV-positive MSM (10) amidst intermittent antiretroviral (ARV) stockouts and broader challenges in access to ARV for low socioeconomic Thais and migrant workers living with HIV (11,12). Along with a context of discrimination against YMSM and transgender women in health care settings (13), these factors underscore the implementation challenges of scaling up treatment for key populations in Thailand. In this high risk environment, it is vital to support a renewed emphasis on innovative prevention approaches that are acceptable to YMSM and transgender women, including those who engage in sex work.

Notwithstanding the demonstrated efficacy (14) and effectiveness (15) of daily oral pre-exposure prophylaxis (PrEP), and emerging evidence for the effectiveness of intermittent (event-driven) PrEP (16), a topical rectal microbicide may have biological and behavioral advantages over oral PrEP. On a biological level, it has been suggested that a microbicide may be able to achieve high drug concentrations in local tissue, not achieved with oral PrEP, which may limit systemic exposure along with potential toxicities and resistance (17,18), possibilities that will be evaluated as trials continue. On a social-behavioral level, daily (or even intermittent) pill dosing for prevention may be encumbered by a number of barriers—as indicated by suboptimal adherence in the iPrex trial (14). Challenges for adherence may be exacerbated in resource-limited settings with existing barriers in access to ARVs and pervasive HIV stigma. Some of the substantial barriers to PrEP uptake and adherence may be mitigated by a topical product, which might also serve as a lubricant and may be more acceptable to YMSM and transgender women at risk for HIV infection (19,20).

Nevertheless, correct and consistent usage is key to the effectiveness of topical microbicides. With the past two decades of microbicide research focused on vaginal transmission, relatively fewer studies have focused on the acceptability of rectal microbicides. However, important lessons from vaginal microbicide research include challenges around adherence, an ongoing problem in vaginal microbicide trials resulting in low product efficacy (21-23). Microbicide researchers have called for more sophisticated social and behavioral investigations to assess end users' preferences in order to inform product development (24,25). The growing inclusion of behavioral measures of acceptability and adherence in the context of biomedical HIV prevention trials, including rectal microbicide trials (e.g., MTN017) (26,27), offers an important

complement to efficacy studies. In addition to helping to understand product efficacy in trials, such data offer preliminary evidence to help bridge the ubiquitous research-to-practice gaps that characterize attempts to scale-up of biomedical innovations in health (28,29). Nevertheless, it is important to acknowledge limitations in generalizing social and behavioral data from select participants in controlled clinical trials (with free products, ongoing prevention counseling, adherence monitoring, social support, healthcare provisions, financial incentives, etc.) to key populations and real-world conditions for which the appropriate “laboratory...is the community” (29, p. 211). The triangulation of social and behavioral data from within and outside of clinical trials may generate evidence that best addresses the tremendous challenges of product implementation (30).

Earlier Phase 1 rectal microbicide studies, largely conducted among gay men in the US, assessed rectal administration of products intended for vaginal use, with suboptimal outcomes (17,26,31,32). Presently, rectal microbicide development and clinical trials are in progress based on products designed for rectal or dual compartment use (26,33). A Phase 1 study (MTN-007) conducted in the US (34) indicated that a reduced glycerin (5% versus 20%) formulation of tenofovir gel (RG-TFV 1%) was safe and well tolerated, with less gastrointestinal side effects than a more hyperosmolar vaginal formulation when used rectally (35). The reduced glycerin formulation is being tested in a Phase 2 expanded safety study (MTN-017) with MSM and transgender women in Peru, South Africa, Thailand and the US (26,27).

Initial studies of hypothetical rectal microbicide use among YMSM, aged 18 to 30 years, suggest high (82-88%) uptake in a trial context; however, 40 of 95 YMSM reported using the product

inconsistently for receptive anal intercourse (36). A study comparing the use of different rectal microbicide delivery systems among men and women for both anal and vaginal intercourse revealed that 43% used a study-provided gel applicator in the previous 2 weeks, with different product preferences by gender (37). Both gender and cultural preferences may be expected to impact on rectal microbicide acceptability, in part as product use may be contingent on sexual partners and social norms (17,38). Differences in preferences for rectal microbicides also might be expected between YMSM and transgender women, and among those engaged in sex work, although to the best of our knowledge these factors have not previously been assessed.

With a clear need for the meaningful engagement of end users, particularly YMSM and transgender women, in the development of new biomedical prevention technologies to support combination packages that are acceptable (39,40), we assessed preferences and acceptability of hypothetical rectal microbicides among a community sample of YMSM and transgender women in two Thai cities.

METHODS

Survey Participants

In collaboration with community-based organizations (CBOs) in Chiang Mai and Pattaya that serve MSM or transgender women, including male and transgender service (sex) workers, we recruited a community sample of YMSM and transgender women. We implemented venue-based sampling of survey respondents in go-go bars, host bars, massage parlors/spas, a gay volleyball site, and CBO offices. Inclusion criteria were being MSM or transgender, between the ages of 18 and 30 years, and able to understand Thai language. In order to ensure sampling of YMSM and

transgender women engaged in sex work, we conducted recruitment among staff in commercial venues (i.e., go-go bars, host bars, massage parlors), many of whom engage in sex for money. We did not conduct recruitment among clients in commercial venues.

In collaboration with a CBO representative, Thai research staff approached owners or managers of all potential venues to explain the study, procedures, and seek approval to conduct recruitment on site. In the case of commercial venues, we arranged mutually agreeable times to conduct recruitment before business hours in order to enhance privacy. Site managers informed potential participants about the study. Those who indicated interest were then individually informed about the study by trained Thai community research staff who emphasized the voluntary nature of participation, that participating or not would have no bearing on employment or receipt of CBO services, and confidentiality. The study and consent procedures were approved by the HIV/AIDS Research Ethics Board of the University of Toronto, with administrative approvals from MPlus+ (Chiang Mai) and Take Care!! (Pattaya). All survey participants provided written informed consent using only their initials in order to protect anonymity.

Data Collection

We used Tablet-Assisted Survey Interviewing (TASI) in Thai. Questionnaire items were based on our preliminary qualitative research (20), and published research on rectal microbicide development (27) and preferences (41), and acceptability of other biomedical HIV prevention technologies in Thailand (42,43). We programmed the survey questionnaire, including a choice elicitation task—an experimentally constructed choice scenario in which a respondent identifies a preferred microbicide alternative from a given set—using Java for Android with Eclipse. A

choice scenario refers to a set, in this case, of 5 hypothetical rectal microbicide cards; an alternative refers to a particular rectal microbicide card in the choice scenario. The questionnaire was self-administered in Thai language on Android tablet devices, with trained Thai research staff on hand to respond to questions or assist with administration.

Survey items addressed sociodemographic characteristics (age, gender, education, employment status, and income), engaging in sex work, and acceptability and attitudes towards hypothetical rectal microbicides. We used a choice elicitation task to estimate rectal microbicide preferences, and to model potential differences by sex work (versus no sex work) and by gender (YMSM versus transgender women).

We created hypothetical rectal microbicide scenarios using a Bayesian D-error minimizing design with dummy coded variables obtained with Ngene software (ChoiceMetrics, Sydney, Australia). The basic principle behind the Bayesian approach is akin to practical situations in which we often have some prior information about a parameter to be estimated; alternately, in a non-Bayesian approach, nothing is assumed to be known about the parameter in advance of the information contained in the data. Bayesian analysis, used with increasing frequency in pharmacoeconomics (44) and health economics (45), differs from classical statistical analysis in that it builds on previously determined probabilities and probability distributions of utility coefficients—the weight with which each product attribute contributes to total utility, or value, for a given product (46,47). Thus Bayesian analysis takes into account prior information and current choices from experimental data, while also accounting for uncertainty. A Bayesian efficient design (one type of which is the D-error minimizing design that we employ) allows the

researcher to incorporate information on an a priori distribution of parameters to minimize the probability of error (48), thus increasing reliability and statistical power of the analysis at viable sample sizes. More specifically, Bayesian D-error minimization is a procedure by which a subset of the full factorial design is chosen so as to provide an efficient estimate (i.e. one with low variance), incorporating empirically informed priors—estimates based on relevant previous data that are used to inform model coefficients (49). The goal of this method is to create an optimal design for providing accurate assessments of participant preferences (49) for different hypothetical rectal microbicide products and particular attributes of rectal microbicides.

To support the design of the discrete choice experiment, we obtained empirically informed priors for model coefficients from an initial qualitative study (5 focus groups; n=37) (20) and a subsequent pilot study of the choice elicitation task (n=24) administered on laptop computers (CASI). The pilot study demonstrated the feasibility of the choice elicitation method with our population and provided empirically informed priors for Bayesian analysis that were incorporated in the final survey, as well as ensuring the validity and logic of the experimental design. The pilot study also suggested potential differences in rectal microbicide preferences by sex work and gender, which we then used to inform the final survey design.

The final design included 32 choice scenarios of 5 hypothetical rectal microbicide alternatives, each blocked in 4 groups of 8 choice scenarios in order to reduce the cognitive burden on survey respondents (50). In the choice elicitation task, survey respondents double-ranked, best-worst, 8 sets of 5 rectal microbicide cards, each consisting of 5 dichotomous attributes: gel or suppository; 99% or 50% effective; intermittent dosing (prior to sex) or daily dosing;

prescription or over-the-counter; and cost 20 Thai baht (THB) (\$0.60 USD) or 250 THB (\$7.60 USD) (see Appendix A). For reference, 20 THB is the approximate cost of a Thai condom. We used “99% effective”, although unlikely to be realized in practice, to establish a clear referent for a partial (i.e. “50% effective”) efficacy product, based on methodological recommendations for choice elicitation tasks (51,52); we aimed to make the numerical alternatives easily comprehensible to participants with low educational attainment. Trained interviewers explained gel formulation (“gel” or “lube” in Thai) as being similar to existing gels, familiar to respondents, that are applied by hand or with fingers and used for anal sex. The suppository (“insert drug” in Thai) was described as potentially tablet shaped, which would be inserted into the anus where it would dissolve, similar to familiar rectal or vaginal delivery methods for some medications.

After a practice choice task on the tablet, 5 microbicide cards appeared on the screen; participants were instructed to choose the best and worst, which they then dragged and dropped in a box on the upper left (“best”) and upper right (“worst”) of the tablet screen (see Figure 1). Participants repeated the best-worst task with the remaining 3 rectal microbicide cards, with the final (fifth) card assigned by default to 3rd place. This procedure was repeated 8 times. The design of the instrument follows World Health Organization best practice (53), and similar choice elicitation tasks have previously been conducted in Thai populations (54). The average time to total survey completion was 33 minutes (range 25 – 45 minutes).

Insert Figure 1 here

Data Analysis

We used descriptive statistics to characterize the sample demographics. As YMSM who engage in sex for money or other commodities often do not identify as sex workers (5), nor is the formal employment agreement of those who work in gay entertainment venues designated as sex work, we defined engaging in sex work based on an affirmative response to either of the following two questions: In the past 3 months, how often have your sex partners paid you for sex?; and, In the past 3 months, how often have your sex partners given you drugs, food, or a place to stay in exchange for sex? Among those who declined to respond to one or both questions, 33 who indicated their primary employment at a commercial gay entertainment venue were also classified as having engaged in sex work. Anecdotally, among those employed at gay entertainment venues, a range of different agreements may exist: some may work full- or part-time at a bar from which they draw a monthly salary and share the proceeds from clients, while others may draw no salary from the venue but pay a small fee per client for using the venue as a base. Others who draw a basic salary working as masseuses may supplement their income with tips from clients on the premises.

We compared hypothetical rectal microbicide acceptability and attitudes by sex work and by gender using Fisher's exact test. We analyzed full-rank data (i.e., including all choice alternatives, rather than only best-worst) from the choice elicitation task based on random utility theory, which provides a framework for rational behavior in choice (55). According to random utility theory, participants choose the alternative among available choices that they believe will provide them with the highest value or utility. Other paradigms are available, such as elimination-by-aspect or random regret minimization. However, random utility theory provides

the advantage of representing a reasonable behavioral paradigm and at the same time being consistent with economically sound welfare estimates (55). In a choice context, value is revealed indirectly by making comparison across alternatives that differ in their relevant attributes, which include cost. This value revelation mechanism is quite intuitive and involves a lower cognitive burden for participants than alternative value revelations based, for example, on statement of maximum willingness-to-pay.

We estimated random utility logit likelihood functions, which take into account participants' choices among multi-attribute rectal microbicide alternatives in each choice scenario, with custom routines in Gauss programming language (Aptech Systems Inc., Arizona, US). Gauss, designed for use with matrices, supports a broad range of econometric analyses that may require customization, apropos of our study design. Earlier discrete choice experiments in health were predominantly based on binary models limited to two 'forced' alternatives, for which binary logit or probit models are appropriate. Based on our design, with 5 multi-attribute rectal microbicide alternatives in each choice scenario, we fitted full ranking data to a multinomial logit likelihood function using the rank-exploded logit model (56). The exploded logit model, based on random utility theory, has been used extensively in marketing research (56). We then evaluated the trade-off between other attributes and cost in terms of probability of acceptance at any given cost, following Cameron et al (57). The marginal willingness-to-pay—the contribution to overall willingness-to-pay related to one of the attributes of the hypothetical rectal microbicide—for each microbicide attribute was estimated by taking the ratio of the estimated coefficient on each microbicide attribute to the estimated coefficient on cost. From these marginal willingness-to-pay estimates, a mean willingness-to-pay and associated approximation of a confidence interval

can be estimated for any combination of microbicide attributes. We estimated the marginal effects on utility of the microbicide attributes using NLOGIT (Econometric Software, Inc., New South Wales, Australia). Coefficients were converted to odds ratios to aid interpretation.

We ran two multinomial logit models. The first estimates overall marginal willingness-to-pay for the sample as a whole; the second estimates separate marginal willingness-to-pay by gender and by sex work. Both models control for gender (transgender vs. YMSM) and sex work, but not other demographic characteristics of respondents.

RESULTS

From April to August 2013, among 491 YMSM and transgender women contacted, 408 completed the survey. Fifty were ineligible: 34 were over 30-years-old and 16 arrived after the pre-arranged interview time period. Among the 441 deemed eligible, 25 declined to participate, 7 didn't speak Thai, and 1 was too intoxicated, for an overall response rate of 92.5%. Overall, 212 indicated being paid for sex and 57 had received drugs, food, or a place to stay in exchange for sex. Combined, 259 of the 408 participants (63.4%) were identified as engaging in sex work.

Table 1 summarizes the demographic characteristics of the sample and differences by sex work and gender. Three-quarters (74.5%) were men and one-quarter (25.5%) transgender women, with an overall mean age of 24.3 years (median = 24 years). Over one-third (35.5%) of participants had 9th grade or less education. The median monthly income was 9,406 THB (\$285 USD); 41.7% earned less than 7,500 THB (\$227 USD) per month, less than Thai minimum wage (58).

YMSM and transgender women engaged in sex work had significantly lower education than those not engaged in sex work; transgender participants had significantly higher education than YMSM. Those involved in sex work were significantly more likely to report that they worked full-time and significantly less likely to report that they were unemployed. Transgender women were significantly less likely to report that they worked full-time and more likely to report that they were unemployed than YMSM. Participants engaged in sex work had significantly higher income than those not engaged in sex work, with no significant difference in income by gender.

Insert Table 1 here

Overall, 83.4% reported they would definitely use a rectal microbicide. Table 2 compares acceptability and attitudes between those engaged in sex work and those not, and between YMSM and transgender women (“don’t know” responses are excluded). Early adoption of a rectal microbicide (82.5% overall) was significantly higher among those involved in sex work (85.2%) than those not involved in sex work (76.9%, $p=0.029$). Notably, overall acceptability was 65.3% if a rectal microbicide had to be combined with condom use and 38.4% if a rectal microbicide caused mild temporary side effects, with no significant differences by sex work or gender.

Participants engaged in sex work were significantly more likely than those not engaged in sex work (56.9% versus 39.9%, $p=0.002$) to be afraid they might contract HIV. YMSM were significantly more likely than transgender women (56.8% versus 40.8%, $p=.007$) to want their

partner to know that they use a rectal microbicide, but did not differ across other attitudinal questions.

Insert Table 2 here

The results from the full rank model, in terms of estimated impact on microbicide choice, are presented in Table 3. All microbicide attributes are significant at the 1% level. Efficacy is the microbicide attribute with the greatest marginal effect on choice: on average, participants have more than two times higher odds of choosing a microbicide with 99% efficacy than a microbicide with 50% efficacy. A gel formulation increases the odds of choice by more than 40 percent compared with a suppository. Intermittent use before sex increases the odds of choice by nearly 30 percent compared with daily use. Participants prefer microbicide availability by prescription rather than over-the-counter, with prescription increasing the odds of choice by nearly 20 percent compared with over-the-counter.

The final column in Table 3 shows the results when converted to marginal willingness-to-pay, obtained by taking the ratio of the estimated coefficient on each microbicide attribute to the estimated coefficient on cost. On average, participants would be willing to pay 1471 THB (\$45 USD) more for a microbicide with 99% efficacy than one with 50% efficacy, 668 THB (\$20 USD) more for a microbicide with a gel formulation than a suppository, and 504 THB (\$15 USD) more for intermittent use than daily use.

Insert Table 3 here

Table 4 presents the results including interactions between each rectal microbicide attribute and sex work, and with gender. Interaction terms with coefficients found to be statistically insignificant ($p > .1$) were excluded from the final model presented in the table, in line with most of the literature on willingness-to-pay. As indicated by the significant coefficients for the interaction terms (e.g., “99% Efficacy * Sex work”), for participants engaged in sex work, higher efficacy was less important than for non-sex workers. Similarly, for participants engaged in sex work, daily dosing rather than intermittent dosing was more acceptable compared with non-sex workers. In other words, although both those engaged in sex work and those not engaged in sex work preferred higher efficacy and intermittent (rather than daily) dosing, the preferences for higher efficacy and intermittent dosing were greater for non-sex workers. The only significant interaction for YMSM was for dosing: compared with transgender women, YMSM rated intermittent dosing significantly more acceptable (rather than daily dosing). In other words, although both groups preferred intermittent use before sex, this preference was more apparent for YMSM than for transgender women. As expected, the pattern of marginal willingness-to-pay results closely follows the odds ratios.

Insert Table 4 here

Figure 2 expands on these results by showing the marginal willingness-to-pay results separately for all four groups in the sample (sex workers and non-sex workers, and YMSM or transgender

women). These results combine the marginal willingness-to-pay results from Table 4, and show the difference in willingness-to-pay between a microbicide having all the most preferred attributes, and one having all the least preferred attributes, for each group. For instance, for YMSM engaged in sex work, the overall difference in willingness-to-pay between a microbicide with all the most preferred attributes and one with all the least preferred attributes is 2,827 THB (\$86 USD) (represented by the overall length of the bar). This is made up of 677 THB (\$21 USD) willingness-to-pay for the gel formulation rather than a suppository, 1,283 THB (\$39 USD) willingness-to-pay for 99% efficacy rather than 50% efficacy, 519 THB (\$16 USD) willingness-to-pay for intermittent dosage rather than daily dosage, and 349 THB (\$11 USD) willingness-to-pay for prescription rather than over-the-counter availability. Overall, YMSM non-sex workers are most willing to pay for the most preferred microbicide (99% efficacy, gel formulation, intermittent dosing, and availability by prescription). In general, sex workers are less willing to pay for the most preferred microbicide than non-sex workers, and transgender women sex workers are least willing to pay of all the four groups.

Insert Figure 2 here

DISCUSSION

Our findings from a community sample of YMSM and transgender women at high risk of HIV exposure in two Thai cities indicate high acceptability of a topical rectal microbicide.

Importantly, this is among the first studies to specifically assess preferences for a hypothetical rectal microbicide, or a new HIV prevention technology in general, among persons engaged in sex work, a key population globally; it is also among the first to disaggregate hypothetical rectal

microbicide preferences of MSM and transgender women, populations often combined in HIV behavioral research.

The high (>80%) acceptability of rectal microbicides in the present study is notable. Although acceptability ratings cannot be directly compared across different studies (given different sampling, recruitment, and data collection methods), it may be helpful to consider that the stated acceptability of PrEP has ranged from 36% among internet-recruited YMSM (n=404) (59), to 39% among YMSM (n=260) recruited across diverse venues in Bangkok and Chiang Mai (43), to 37% among transgender women (n=107) and 41% among YMSM (n=131) recruited from educational and gay entertainment venues in Chiang Mai (60).

The odds ratios in the discrete choice models demonstrate the intensity of preference for different attributes of a hypothetical rectal microbicide. In addition to the over two-fold higher odds of choice for a high (versus partial) efficacy rectal microbicide, YMSM and transgender women indicated 40% higher odds of choosing a gel formulation (versus suppository); the willingness-to-pay 1,471 THB (\$45 USD) more for high efficacy and 668 THB (\$20 USD) more for a gel are substantial given median monthly income of 9,406 THB (\$285 USD). Earlier rectal microbicide studies that used hypothetical products among MSM in NYC similarly revealed a preference for a gel over a suppository (41), and a gel-filled applicator over a suppository or enema (36), albeit with limitations in the volume of gel that would be acceptable (61). Hypothetical rectal microbicide preferences identified in a pilot study with MSM in South America were also similar to those in the present study: higher efficacy, intermittent use before sex, gel formulation, and prescription required (62). The present results build on these past studies by quantifying the

impact of each attribute on acceptability in terms of odds of choice, and allowing direct comparison of the magnitude of preferences in terms of willingness-to-pay.

Interestingly, a preference for a prescription product emerged among South American MSM, similar to the Thai YMSM and transgender women in the present study; in both cases it appears that there may be greater trust in the quality and efficacy of a physician prescribed product (62). In Thailand, medications (often non-prescription) covered under a 30 THB (~\$1 USD) co-pay national health insurance program are generally perceived to be inferior to those available only to people with private insurance, which may further explain the prescription preference. This finding supports the importance of conducting hypothetical rectal microbicide acceptability research in different cultural and economic contexts, particularly in resource-limited settings. Arguably a prescription requirement might not be preferred in the US—particularly among YMSM and transgender women—given the generally high cost of prescription versus over-the-counter medications and barriers posed by having to visit a physician, in a health care system in which many people of low socioeconomic status are uninsured or underinsured.

The present findings also indicate lower sensitivity to differences in hypothetical rectal microbicide characteristics among YMSM and transgender women who engaged in sex work. Those engaged in sex work indicated higher likelihood of accepting a rectal microbicide immediately upon availability, and exhibited more tolerance for a moderate efficacy product and one requiring daily use. Previous investigations have noted the lack of focus on male sex workers as indicating an important direction for rectal microbicide acceptability research (62). Even as those engaged in sex work and those not engaged in sex work both preferred higher efficacy and

intermittent (versus daily) dosing, the greater openness of sex workers to accept non-ideal products appears rational given their greater exposure to HIV based on multiple sexual partners and the occupational hazards of sex work. Sex workers in the present study perceived higher risk of HIV infection than those not engaged in sex work. More consistent sexual activity on the part of those who engage in sex for money or goods also may help to explain greater tolerance of products requiring daily use. The significantly higher reported likelihood of accepting a rectal microbicide immediately upon availability, greater tolerance for non-ideal products, and higher perceived HIV risk among those engaged in sex work also suggest that YMSM and transgender female sex workers may be among “early adopters” and “early majority” adopters of rectal microbicides, in accordance with Diffusion of Innovations Theory (63). Sex workers may have particular motivation to use a rectal microbicide and are likely to perceive relative advantages of rectal microbicide use over existing alternatives—based on perceived HIV risk and sustained occupational exposure—characteristics that are generally associated with early adopters (63-65). Focusing on these potential early adopters may be an effective social marketing strategy for encouraging product rollout to broader communities of YMSM and transgender women in Thailand once a rectal microbicide becomes available.

Importantly for future rectal microbicide implementation, YMSM and transgender women involved in sex work were less willing to pay for their preferred products than those with other employment. It is possible that despite their higher reported income, the stability and reliability of sex workers’ earnings from month to month may be less certain than among those engaged in more traditional types of salaried employment; thus they may be more sensitive to cost. Given high HIV prevalence among YMSM and transgender women involved in sex work, our findings

suggest that cost subsidies for rectal microbicides that render them similar in price to condoms (with free availability in CBOs) may represent a significant intervention to support product uptake and adherence among these key populations.

Overall, we did not identify substantial gender differences in hypothetical rectal microbicide acceptability or preferences between YMSM and transgender women. However, the demographic findings indicate that despite the higher educational attainment among young transgender women than YMSM in this sample, transgender women were more likely to be unemployed or under-employed than YMSM; transgender women also indicated lower willingness-to-pay for preferred rectal microbicide attributes, which may be interpreted in part as a function of economic constraints. Among the manifestations of stigma against transgender people, documented in Thailand as elsewhere, is that it restricts employment opportunities (66,67). Gender differences emerged in lesser willingness on the part of transgender women than YMSM to have their partner know they were using a rectal microbicide. This may be a function of transgender women wanting to please ostensibly heterosexual male partners and perceived concerns about their rectal microbicide use among male partners.

Limitations

Limitations to this study include the nonprobability sampling; caution should be observed in generalizing findings to other YMSM and transgender women in Thailand. Although alternative approaches such as respondent-driven sampling (RDS) have the potential to achieve greater generalizability than venue-based sampling, evaluations of RDS suggest it may result in biased population estimates, requiring samples in the thousands to achieve the level of precision often

presumed (68,69). Moreover, we chose venue-based sampling based on our aim of recruiting YMSM from gay entertainment venues, including a substantial sample of male sex workers; RDS, a chain-sampling method, affords the researcher less control over the sample making it more dependent on the initial participants selected as seeds (68). Furthermore, it is challenging to define sex work among YMSM and transgender women, which is not necessarily equivalent to sex work by women; many YMSM who engage in transactional sex do not identify as sex workers (5). By design, the present sample of YMSM and transgender women may be at higher risk for engaging in sex work and for HIV acquisition, indicative of those employed in the gay entertainment industry and some who seek services from HIV prevention organizations, than the broader population of YMSM and transgender women in Thailand. However, we successfully recruited a community sample of high-risk YMSM and transgender women in diverse venues in two cities, a majority of whom engaged in transactional sex; and this is among the first studies to compare acceptability and preferences for hypothetical rectal microbicides between MSM and transgender women, and between MSM and transgender women engaged in sex work versus not engaged in sex work.

As in any experimental investigation, we are only able to assess the systematic impact of those attributes used in the experimental design and modeled from the choice experiment data; in practice, additional product features, such as applicator type, volume, color, and potential side effects, may impact on rectal microbicide preferences (20). It is plausible, for example, that if a future gel-based microbicide required an applicator, it might be less preferred as a formulation than in the present analysis. A common challenge of discrete choice experiments, while having many advantages over traditional single-item measures of preferences for discrete product

attributes and over choice-based conjoint analysis designs that artificially presume orthogonality (i.e. main effects of each attribute with no interaction effects) (70), is to balance the number of attributes modeled with the cognitive burden on respondents (71). Furthermore, it may be helpful in future investigations to directly compare the acceptability of different biomedical prevention products. As rectal microbicides may become available in the context of an evolving landscape of other biomedical HIV prevention modalities, such as oral pre-exposure prophylaxis (PrEP), these may influence product preferences. The inclusion of multiple products in discrete choice experiments, however, must be balanced against the increased cognitive burden, particularly in different cultures and languages, and in low- and middle-income countries among populations that may have lower literacy and less exposure to market research techniques (72). Additionally, we prioritized the ability to detect differences within key populations, and this is among the first discrete choice experiments in HIV prevention to disaggregate findings among MSM and transgender women, and by sex work, an urgent priority for future research on biomedical HIV prevention (73).

Overall, as in any acceptability research, stated preferences and willingness-to-pay for hypothetical products do not equate with actual product uptake, but are robust methods for assessing consumer preferences prior to product availability (44,71) to support evidence-informed implementation. We used focus groups, translation/back-translation and a pilot survey to inform product descriptions in Thai language, but did not employ hypothetical product prototypes or pictorial cards, which may be beneficial in future research on hypothetical rectal microbicide acceptability among key populations. Finally, our models controlled for gender and sex work, in accordance with study objectives, but other demographic factors, such as income,

may contribute to differences between groups. Further research conducted—both within and outside of clinical trials—as rectal microbicide development advances, and product attributes as yet unknown are determined, will build on the present results to support rectal microbicide introduction and dissemination.

CONCLUSIONS

Our findings indicate high acceptability of rectal microbicides among YMSM and transgender women in Thailand, supporting the vital importance of sustained rectal microbicide research and development. They also demonstrate the importance of conducting social and behavioral research on new prevention technologies focused on sex workers, and disaggregating the preferences of MSM and transgender women. It may be that one rectal microbicide does not fit all (17). Tailoring biomedical research to the extent possible to address the preferences of key HIV prevention end users, and preparing for evidence-informed social marketing interventions to support rectal microbicide uptake in key populations, including YMSM and transgender women in resource-limited settings, may optimize the effectiveness of rectal microbicides in slowing the HIV epidemic.

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